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10/692,011	10/24/2003	Kenji Nakajima	Q78108	8536

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EXAMINER	
LUM, LEON YUN BON	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 05/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/692,011	NAKAJIMA, KENJI	
	Examiner	Art Unit	
	Leon Y. Lum	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *1,4,7,10 and 13-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,3,5,6,8,9,11 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed 22 February 2005 is acknowledged and has been entered.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 2-3, 5-6, 8-9, and 11-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4. In claims 2-3, line 6 of the claims, the phrase "a receptor or a ligand" is vague and indefinite. It is not clear whether the receptor and ligand in the instant phrase is the same as or different from the ligands and receptors recited in the preceding phrase "to which ligands or receptors have been bound" (lines 4-5).

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 2-3 and 5-6 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Besemer et al (US 6,140,044).

In the instant claims, Besemer et al reference teaches an array of probes (i.e. bound ligands or bound receptors) on a wafer (i.e. biochemical analysis unit), wherein the wafer may contain depressed regions and surfaces on the wafer can be membranes (i.e. porous adsorptive regions), and wherein the wafer can be mounted in a 96-well microtiter format for parallel hybridization (i.e. plurality or regions). See column 5, line 41 to column 6, line 3; column 15, lines 57-67; and Figure 1a. In addition, Besemer et al teach the step of connecting the chip to a fluid delivery system that introduces fluids to contact the probes during the hybridization process (i.e. forcibly causing a receptor or ligand to flow across each of the porous adsorptive regions), wherein the fluid contains labeled targets (i.e. labeled receptor or labeled ligand; utilization of a labeling substance) that will hybridize with only complementary sequences on the substrate, and wherein reactions between the probes and targets are analyzed by imaging systems (i.e. detecting the receptor or the ligand). See column 1, lines 24-40; column 12, lines 49-57; and column 13, lines 21-23. Furthermore, Besemer et al teach the step of removing bubbles (i.e. bubble removing and dissolving process) from the cavity by placing inlets and outlets at the highest and lowest positions in the cavity, respectively. See column 8, lines 13-15.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. Claims 8-9 and 11-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Besemer et al (US 6,140,044) in view of Bronstein et al (US 5,543,295).

Besemer et al reference has been disclosed above and additionally teaches that the targets (i.e. receptor or ligand) can be nucleic acids and can be labeled with an enzyme (i.e. auxiliary substance). See column 4, line 6; and column 3, lines 50-60.

However, Besemer et al fail to teach the step of forcibly causing a reaction liquid containing a labeling substance, which is capable of undergoing specific binding with the auxiliary substance, to flow such that the reaction liquid flows across each of the porous adsorptive regions of the biochemical analysis unit, the labeling substance,

which is capable of undergoing specific binding with the auxiliary substance, thus being specifically bound to the auxiliary substance-bound receptor or the auxiliary substance-bound ligand having been specifically bound to at least one of the bound ligands, or to at least one of the bound receptors, and detecting the auxiliary substance-bound receptor or the auxiliary substance-bound ligand, which has been specifically bound to at least one of the bound ligands or at least one of the bound receptors, by the utilization of the labeling substance.

Bronstein et al teach the step of performing specific binding assays between two molecules and then exposing a dioxetane to the bound molecules, wherein an enzyme (i.e. auxiliary substance) tagged on one of the molecules cleaves an enzyme cleavable group on the dioxetane and causes a chromophore (i.e. labeling substance) bonded to the enzyme cleavable group to luminescence and be detected, in order to provide water soluble reporter molecules that can be used in bioassays. See column 17, line 66 to column 18, line 18; and column 2, lines 12-24. In addition, Bronstein et al teach that the enzyme can be bound to nucleic acid. See column 17, lines 62-63.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Besemer et al with the step of performing specific binding assays between two molecules and then exposing a dioxetane to the bound molecules, wherein an enzyme (i.e. auxiliary substance) tagged on one of the molecules cleaves an enzyme cleavable group on the dioxetane and causes a chromophore (i.e. labeling substance) bonded to the enzyme cleavable group to luminescence and be detected, as taught by Bronstein et al, in order to provide water

soluble reporter that can be used in bioassays. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including the steps of Bronstein et al, in the method of Besemer et al, since Besemer et al teach the specific binding of two molecules, wherein one molecule is labeled with an enzyme, and the steps of Bronstein et al produces bioassay detection through the cleavage of a labeling substance that is contacted with an enzyme labeled on one member of a specific binding pair.

Double Patenting

10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. Claims 2-3, 5-6, 8-9, and 11-12 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of copending Application No. 10/649,719 in view of Besemer et al (US 6,140,044).

The instant application recites an assay method using a biochemical analysis unit, comprising the steps of obtaining a biochemical analysis unit provided with a plurality of porous adsorptive regions, to which ligands or receptors have been bound respectively, and performing a specific binding detecting process comprising the steps of forcibly causing a receptor or a ligand to flow such that the receptor or the ligand flows across each of the porous adsorptive regions of the biochemical analysis unit, the receptor or the ligand being thus subjected to specific binding with the bound ligands or the bound receptors, the receptor or the ligand being thereby specifically bound to at least one of the bound ligands, or to at least one of the bound receptors, and detecting the receptor or the ligand, which has thus been specifically bound to at least one of the bound ligands or at least one of the bound receptors, by the utilization of a labeling substance, a liquid being forcibly caused to flow, such that the fluid flows across each of the porous adsorptive regions of the biochemical analysis unit, during the specific binding detecting process, wherein bubble removing processing for removing bubbles, which are present in the liquid, from the liquid is performed during the flowing of the liquid.

The copending application teaches certain limitations of the instant application by reciting a chemical luminescence method using a biochemical analysis unit, comprising the steps of obtaining a biochemical analysis unit provided with a plurality of porous adsorptive regions, to which ligands or receptors have been bound respectively, subjecting a labeled receptor or a labeled ligand, which has been labeled with a labeling substance, to specific binding with the ligands or the receptor (i.e. specific binding

detecting process) s, each of which has been bound to one of the porous adsorptive regions of the biochemical analysis unit, the labeled receptor or the labeled ligand thereby specifically bound to at least one of the ligands or at least one of the receptors, causing a chemical luminescence substrate to undergo a reaction with the enzyme-labeled antibody, which has been specifically bound to the labeled receptor or the labeled ligand (i.e. detecting the receptor or ligand; by utilization of a labeling substance), wherein, at the time at which the enzyme-labeled antibody is subjected to the specific binding with the labeled receptor or the labeled ligand, which has been specifically bound to at least one of the ligands or at least one of the receptors, a reaction liquid containing the enzyme-labeled antibody is forcibly caused to flow such that the reaction liquid containing the enzyme-labeled antibody flows across each of the porous adsorptive regions of the biochemical analysis unit (i.e. liquid being forcibly cause to flow during the specific binding process).

However, the copending application fails to teach the step wherein bubble removing processing for removing bubbles, which are present in the liquid, from the liquid is performed during the flowing of the liquid.

Besemer et al teach the step of removing bubbles from the cavity by placing inlets and outlets at the highest and lowest positions in the cavity, respectively, in order to improve fluid circulation. See column 8, lines 2-15.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of the copending application with the step of removing bubbles from the cavity by placing inlets and outlets at the highest and lowest positions

in the cavity, respectively, as taught by Besemer et al, in order to improve fluid circulation. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including the step of removing bubbles, as taught by Besemer et al, in the method of the copending application since both the copending application and Besemer et al are directed towards fluid flow on substrates for binding assays.

This is a provisional obviousness-type double patenting rejection.

Response to Arguments

12. Due to Applicants' claim amendments and arguments on pages 1-24 of the Remarks, filed 22 February 2005, the rejections under 35 U.S.C. 112, second paragraph made in the previous Office Action have been withdrawn, except for the rejection of claims 2-3 due to the phrase "a receptor or ligand" (line 6). The receptor and ligand of the instant phrase is not clearly distinguished between the receptor and ligand in the preceding lines of the claims, and it is not clear whether the receptors and ligands from both lines are the same or whether they are different.

13. On pages 25-27 of the Remarks, Applicants argue that Besemer et al reference does not teach the claimed invention and specifically, that Besemer et al do not disclose flowing a fluid across the adsorptive region and that generation of bubbles is not a problem in the reference (page 26, 2nd paragraph) and that the bubbles in Besemer et al

and the bubbles in the present invention are completely different in their formation process (page 27, 2nd paragraph).

Applicant's arguments filed have been fully considered but they are not persuasive. As claimed, the present invention is a method that includes the step wherein "the receptor or the ligand flows across each of the porous adsorptive regions of the biochemical analysis unit" (i.e. claim 2). The specification does not define the term "across" and as presented, the claims include any situation wherein liquid contacts the biochemical analysis unit by flow from one side to another. Besemer et al teaches the claimed limitation by reciting a fluid delivery system that introduces fluids to contact the probes during the hybridization process, as stated in the 35 U.S.C. 102(b) rejection supra. Since a fluid delivery system is used to apply fluid, there is inherently a flow of liquid across the probes.

With regards to Applicant's arguments concerning the bubbles, as claimed, the present invention is a method that includes the step "wherein bubble removing processing for removing bubbles, which are present in the liquid, from the liquid is performed during the flowing of the liquid" (i.e. claim 2). The claimed limitation is broad enough to encompass any process for removing any type of bubble within any embodiment since it only requires a bubble removing process during the flow of liquid. Therefore, Applicants' argument that the bubbles in Besemer et al are different from the bubbles of the claimed limitation is not persuasive since the claims do not place a limit on the type of bubbles and does not place a restriction on the type of process that removes the bubbles. The rejection under 35 U.S.C. 102(b) is therefore maintained.

With regards to Applicants' statements that claims 8-9 and 11-12 are patentable over Besemer et al (page 27, 4th paragraph), since it has been determined that Besemer et al has been properly applied against claims 2-3, and Applicants have not argued against the combination of Besemer et al and Bronstein et al, the rejection under 35 U.S.C. 103(a) is therefore maintained.

Conclusion

14. No claims are allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leon Y. Lum whose telephone number is (571) 272-2878. The examiner can normally be reached on weekdays from 8:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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05/13/05